

REMARKS

I. Preliminary Matters

Upon entry of the Amendment, which is respectfully requested, claim 5 will be pending in the application.

Claim 5 is amended to incorporate, in part, the subject matter of claims 6 and 8.

Claims 6-8 are canceled without prejudice or disclaimer.

No new matter is added.

Entry of the Amendment is respectfully requested.

II. Claim to Foreign Priority

Applicants thank the Examiner for acknowledging Applicants' claim for foreign priority under 35 U.S.C. § 119.

The Examiner is respectfully requested to acknowledge receipt of certified copies of the two priority documents, which were filed with the PTO on June 24, 2005.

III. Response to Claim Objections

Claims 6, 7 and 8 are objected to because they depend from claim 1, which was canceled in the Preliminary Amendment dated June 24, 2005.

Without acquiescing to the merits, claims 6-8 are cancelled, thereby obviating the objection to the claims.

Therefore, withdrawal of the objection is respectfully requested.

IV. Response to Rejections of Claims Under 35 USC § 112

Claims 5-8 are rejected under 35 U.S.C. § 112, first paragraph, because the specification allegedly does not reasonably provide enablement for a method of treating a disease associated with lumbago, discopathy, or spondylosis or treatment using protease other than a human derived extracellular matrix protease

Initially, without acquiescing to the merits, claims 6-8 are cancelled.

Claim 5, as currently amended, recites a method of therapy for treating a herniated disc or herniated nucleus pulposus by administering an active ingredient comprising MMP-7.

Applicants respectfully submit that in view of the amendments to claim 5, the § 112 rejection is overcome.

Reconsideration and withdrawal of the § 112, first paragraph rejection is therefore, respectfully requested.

V. Response to Rejection of Claims under 35 USC § 102

Claims 5, 7 and 8 are rejected under 35 U.S.C. § 102(b) as being anticipated by Haro, et al. (*Spine* 22(10):1098-1104 (1997); hereafter Haro I).

Initially, without acquiescing to the merits, claims 7 and 8 are canceled.

Claim 5 is amended to recite an active ingredient comprising MMP-7, which is not disclosed in Haro I.

Therefore, Applicants respectfully submit that Haro I does not teach each and every element of claim 5. Applicants respectfully request reconsideration and withdrawal of the § 102 rejection of claim 5.

VI. Response to Claim Rejection Under 35 USC § 103(a)

Claims 5-8 are rejected under 35 U.S.C. §103(a) as being unpatentable over Einarson, et al. [*Drug Intelligence and Clinical Pharmacy* **18**:560-568 (1984)], in view of Haro I, and Haro, et al. [*Journal of Spinal Disorders* **12**(3):245-249 (1999); hereafter Haro II].

Initially, without acquiescing to the merits, claims 7-8 are canceled.

Claim 5, as currently amended, recites a method of therapy for treating a herniated disc or herniated nucleus pulposus characterized by directly administering an active ingredient comprising MMP-7 to the affected site of the herniated disc or herniated nucleus pulposus. Additionally, MMP-7 is a human derived protease.

In contrast, Einarson describes the use of chymopapain, which is a plant derived protein. Therefore, Einarson neither teaches nor suggests the use of human-derived protease, for e.g., MMP-7.

Furthermore, as described in working Example 3 of the present specification, the nucleus pulposus injected with MMP-7 appears as a degraded matrix, but normal chondrocytes were preserved in the other nucleus pulposus areas and in the annulus fibrosus. In contrast, in the reference Example where chymopapain was used instead of MMP-7, the cartilaginous matrix was degraded throughout the entire nucleus pulposus and annulus fibrosus, with few surviving chondrocytes. Furthermore, when chymopapain is used for treatment, immunoreaction and neurotoxicity have been reported. See page 4 of the present specification.

Haro I evaluates MMP-3 as a chemonucleolytic agent in the treatment of herniated nucleus pulposus. See page 1099, last paragraph to page 1100, left column, line 13 of Haro I. In the experiment described in Haro I, the effect on the annulus fibrosus and chondrocytes around the nucleus pulposus could not be evaluated. In fact, Haro I goes on to state that "obviously,

further research is required as to the effects of stromelysin-1 on annulus fibrosus and endplate, the acute and chronic toxicity on nerve tissue, and long-term roentgenographic changes that occur after intradiscal or epidural administration." See page 1103, left column, lines 22-27 of Haro I. Furthermore, Haro I does not disclose the use of MMP-7.

Finally, Haro II only reports that MMP-7 was expressed in infiltrated mononuclear cells of the granulation tissues of the herniated nucleus pulposus (HNP), and as a result only speculates that MMP-7 may play a role in the resorption process of HNP. See Abstract, Results, and Figs. 1 and 2A of Haro II. Therefore, Haro II does not disclose or suggest the effect of extraneous MMP-7 on herniated discs or herniated nucleus pulposus.

In view of the above, the unexpected and superior properties of the present invention, i.e., the nucleus pulposus injected with MMP-7 appears as a degraded matrix, but normal chondrocytes were preserved in the other nucleus pulposus areas and in the annulus fibrosus, cannot be arrived at by combining Einarson with Haro I or Haro II.

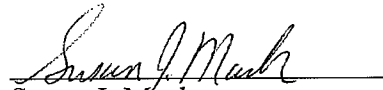
Therefore, Applicants respectfully request reconsideration and withdrawal of the § 103 rejection of claim 5.

Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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CUSTOMER NUMBER

Date: October 30, 2008